UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/092,934	03/08/2002	Paul Averback	018792-0199	7362

22428 7590 01/24/2008
FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
SANG, HONG	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
01/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/092,934	AVERBACK, PAUL	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-52 and 55-60* is/are pending in the application.

4a) Of the above claim(s) *52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-51,55,56, 59 and ,60* is/are rejected.

7)☒ Claim(s) *57 and 58* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Exhibit A*.

DETAILED ACTION

RE: Averback

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/30/2007 has been entered.

2. Clams 47-52, and 55-60 are pending. New claim 60 has been added. Claims 1-46 and 53-54 have been cancelled. Claims 47 and 52 have been amended. Due to applicant's species election of SEQ ID NO.10 (see 8/23/05 response), claim 52 is withdrawn from further consideration as being drawn to non-elected inventions.

3. In the previous office action mailed on 8/22/07, claim 47 wherein the NTP is SEQ ID NO.10 and claim 48 were indicated free of the prior art. This conclusion is hereby withdrawn in view of the newly discovered reference to WO 02/34915A2 (Pub. Date: 5/2/2003, earliest effective filing date: 10/27/2000). Rejections based on the newly cited reference(s) are set forth below (see paragraph 16).

4. Claims 47-51 and 55-60 are under examination. Due to species election, claims are examined to the extent that the NTP is SEQ ID NO.10.

Rejections Withdrawn

5. The rejection of claims 47, 49-51 and new claim 55-59 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a benign tumor, a malignant tumor, hyperplasia, hypertrophy, overgrowth of a tissue and malformation of a tissue in a patient requiring removal or destruction of cells comprising locally administering (e.g. topically, intratumorally) to a mammal in need a therapeutically effective amount of the neural thread protein consisting of SEQ ID NO.10, does not reasonably provide enablement for a method of treating any and all conditions in a patient requiring removal or destruction of cells comprising systemically administering (e.g. intravenously, intra-arterially, intraperitoneally) to a mammal in need a therapeutically effective amount of any and all neural thread protein (NTP) as well as fragments, variant, derivative, homolog, reverse-D peptide, and enantiomers of NTP is withdrawn in view of applicant's amendment to the claims.

6. The rejection of claims 47, 49-51 and new claim 55-59 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicant's amendment to the claims.

7. The rejection of claims 47, 49-51 and 55-59 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-7 of U.S. Patent No. 6,924,266B2 is withdrawn in view of applicant's amendment to the claims.

8. The provisional rejection of claims 47, and 49-51 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-16 and 18 of copending Application No. 10/294,891 and claims 9-13 and 15 of copending Application No. 10/920,313 are withdrawn in view of applicant's amendment to the claims of copending Application Nos. 10/294,891 and10/920,313.

9. The rejection of claims 47, 49-51, 55, and 59 under 35 U.S.C. 102(e) as being anticipated by Xu et al. (US Patent No. 6,620,922B1, Date of Patent 9/16/2003, Filing Date: 8/9/2000) is withdrawn in view of applicant's amendment to the claims.

New Grounds of Objections and Rejection

Claim Objections

10. New claim 60 is objected to because of the following informalities: claim 60 recites "a mammal in need a therapeutically effective amount of a neural thread protein (NTP). However the active method step is administering SEQ ID NO.10 to said mammal. Claims should be amended to recite "a mammal in need a therapeutically effective amount of SEQ ID NO.10 because NTP can be any neural thread proteins, related molecules, as well as biologically active fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers (see page 11, lines 10-11).

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. New claim 60 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 60 recites the limitation "wherein the NTP is administered at the site of the cells". There is insufficient antecedent basis for this limitation in the claim. The active step is "administering SEQ ID NO.10 to a mammal".

Moreover, it is unclear whether other NTP molecules are to be administered in addition to SEQ ID NO.10.

Claim Rejections - 35 USC § 112, 1st paragraph, 1st paragraph

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claim 60 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Claim 60 is rejected because the NTP recited in claim 60 is not limited to the SEQ ID NO.10. Moreover, the claim recites the phrase "the NTP is administered at the site of cell". The NTP recited in the claim is interpreted as any and all NTP molecules. The specification teaches that the NTP refers to a neural thread proteins and related molecules, it also includes biologically active fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers (see page 11, lines 10-11). However, the written description in this instant case only sets forth AD7C-NTP (SEQ ID NO: 10), and the proteins identified by SEQ ID NOS. 2-9. Therefore the written description is not commensurate in scope with the claim which is drawn to a method of treating comprising administering any and all NTP molecules. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The compound itself is required. See

Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Although these court findings are drawn to DNA art, the findings are clearly applicable to the claimed proteins.

Vas-cath Inc. 1. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Furthermore, although drawn specifically to the DNA art the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly applicable to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B (1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). Although the instant specification discloses AD7C-NTP (SEQ ID NO: 10), and the proteins identified by SEQ ID Nos. 2-9, it fails to provide information about the structures and biological functions of any fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers of the SEQ ID NOS. 2-10. Moreover, the instant claims encompass fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers which may not still have the biological function of neural thread peptides. Therefore, the specification provides neither a representative number of fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers of the SEQ ID NOS. 2-10, nor does it provide a description of structural and functional features that are common to the fragments, homologs, variants, derivatives, peptide mimetics, reverse-D peptides, and enantiomers of the SEQ ID NOS. 2-10. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant and encompasses proteins yet to be discovered, the disclosure of the specific species of genus is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 47-51, 55-56, and 59-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/34915A2 (Pub. Date: 5/2/2002, earliest effective filing date: 10/27/2000), in view of Senter (US Patent No.4,874,779, Date of Patent: 10/17/1989), and Xu et al. (US Patent No. 6,620,922B1, Date of Patent 9/16/2003, Filing Date: 8/9/2000).

WO 02/34915A2 teaches a method of treating brain cancer such as neuroectodermal tumors, glioblastomas, and astrocytomas comprising administering to a mammal in need a therapeutically effective amount of one or more Harlil peptides, and Harlil mimetics (see page 7, lines 24-28). The Harlil peptides encompass the full length NTP (see page 9, and claim 9). WO 02/34915A2 teach a method of using a peptide as an analogue for NTP in a therapeutic or diagnostic assay, comprising replacing NTP with the peptide in such an assay, wherein the peptide has an amino acid sequence of HARLIL (see claim 35). WO 02/34915A2 teaches the amino acid sequence of the full length NTP (see Example 1 and Fig.1), which is 100% identical the instant SEQ ID NO.10 (see sequence alignment Exhibit A)

WO 02/34915A2 does not teach administering Harlil peptides to the site of the brain tumor. WO 02/34915A2 does not teach that the Harlil peptides are administered

together with other pharmaceutical compositions. However, these deficiencies are made up for in the teachings of Senter and Xu et al.

Senter teaches a method of treating a tumor using mitomycin derivatives (see abstract). Senter discloses that the cancer drug can be administered by conventional routes including, but are not limited to, intravenous, intramuscular, intratumoral, intraarterial, intralymphatic, and oral.

Xu et al. teach a method of treating cancer comprising administering a polypeptide, wherein the polypeptide can be administered in together with an immunostimulant such as cytokines GM-CSF, or interleukin-2, IL-7, or IL-12 (see column 69, lines 36-38).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer Harlil peptides intratumorally in combination of an immunostimulant such as GM-CSF to treat brain cancer in view of the teachings of WO 02/34915A2, Senter and Xu et al. One would have been motivated to do so because intratumoral administration is a conventional route for administering cancer drugs as shown by the teachings of Senter, and administration of an immunostimulant such as GM-CSF can further enhance the cancer drug effect. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to administer Harlil peptides intratumorally in combination of an immunostimulant such as GM-CSF because such administration methods are well known in the art.

Conclusion

17. Claim 47-51, 55, 56, 59 and 60 are rejected. Claims 57-58 are objected to as being dependent from rejected claims

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hong Sang
Art Unit 1643
1/9/2008

/Christopher Yaen/
Primary Examiner
Art Unit 1643
January 18, 2008